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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,421	03/12/2004	John Devane	09487.0003-00	6571

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,421	DEVANE, JOHN	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,9-37,39-42 and 44-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,9-37,39-42 and 44-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's Request for Continued Examination (RCE) under 37 CFR § 1.114 filed August 31, 2007 is acknowledged and accepted. Claims 2, 7, 8, 38 and 43 are canceled. Claims 1, 3-6, 9-37, 39-42 and 44-77 remain under consideration.

Applicant's Response to an Election of Species Requirement, filed December 28, 2007, is further acknowledged. Upon reconsideration, the Election Requirement is withdrawn. Mecamylamine, N-2,3,3-tetramethylbicyclo-[2.1.1]heptan-2-amine, has been known for decades in the pharmaceutical art as an agent that decreases gastrointestinal propulsion. Accordingly, claims 1, 3-6, 9-37, 39-42 and 44-77 are examined in their entirety.

Although referenced in Applicant's Response filed August 31, 2007, no substitute specification is noted.

Applicant's arguments presented in response to the last Office Action have been considered. Those objections and/or rejections not herein reiterated are withdrawn. The following objections and rejections constitute the only ones presently applied to the instant claims.

The disclosure is objected to for the following informality: Lines 8-9 of claim 30 recite "a peak:trough plasma level **ration**."

Appropriate correction is required.

Claims 39 and 42 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in

proper dependent form, or rewrite the claims in independent form. Intended use confers no patentable weight to composition claims.

Claims 39 and 42 recite an intended use, such as minimizing a side effect or a desired dosing regimen, without reciting a specific chemical or physical property of the formulation of claim 30 from which they depend. Accordingly, claims 39 and 42 do not further limit the subject matter of claim 30.

Claims 1, 3-6, 9-37, 39-42 and 44-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 25 recites "enriched N-2,3,3-tetramethylbicyclo-[2.1.1]heptan-2-amine." Claim 26 recites "substantially pure N-2,3,3-tetramethylbicyclo-[2.1.1]heptan-2-amine." Both claims lack clear antecedent basis in claim 23 from which they depend.

The recitation in claims 1, 30 and 65 "less than about 4:1" (and "less than about 3:1" in claim 44 and "less than about 2:1" in claim 45) with respect to a peak:trough plasma level ratio is indefinite. The recitation encompasses zero.

Clarification is required.

Claims 1, 3-6, 9-37, 39-42 and 44-77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, Applicant must convey with

reasonable clarity, as of the filing date, that Applicant was in possession of the claimed invention. The issue of a lack of adequate written description also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996), (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); *In re Ruschig*, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

Possession may be shown in many ways. For example, possession may be shown by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that Applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. For example, a specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claims and determined that the invention would work for its intended purpose. An Applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that Applicant was in possession

of the claimed invention as a whole.

An Applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics that provide evidence that Applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

In the instant case Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. In Example 1, page 74 of the specification, a hypothetical situation is described drawn to subjects diagnosed with increased gastrointestinal motility due to irritable bowel syndrome (IBS). On pages 82-83 of the specification in Example 7, another hypothetical situation is described for subjects diagnosed with diarrhea-dominant irritable bowel syndrome. Applicant states the formulations disclosed in the specification comprising N-2,3,3-tetramethylbicyclo-[2.1.1]heptan-2-amine demonstrate efficacy in improving IBS symptoms and a dissociation of gastrointestinal motility effects from effects on other systems, including blood pressure, heart rate, vision and bladder function. No such conclusions with respect to "minimizing at least one side effect associated with the administration of a conventional formulation of N-2,2,3-tetramethylbicyclo-[2.1.1]heptan-2-amine", as recited in instant claim 5, are noted. The skilled artisan in gastroenterology would reasonably require a more detailed description of minimization of side effects. There is no description in the instant specification to provide support for minimizing any side

effect, such as those relating to heart rate, blurred vision, bladder function or blood pressure.

Further, there is no description in the instant specification to provide support for any of the claimed pharmacokinetic and pharmacodynamic limitations of the present claims. Although working examples are not required, in the present case there is no description that would provide support to one of ordinary skill in the art an embodiment that meets all the limitations of the claims.

Applicant argues the reasoning for a lack of written description is mere conclusory statements.

The MPEP states that the purpose of the written description is to ensure that the inventor had possession, as of the filing date of the application, of the subject matter defined by the claims.

"To fulfill the written description requirement, a patent Specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

A required description of the numerous and specific pharmacokinetic and pharmacodynamic limitations recited in the claims is absent. One skilled in the art would not have immediately envisaged the claimed limitations in the instant methods, formulations and transdermal formulations.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 9-37, 39-42 and 44-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shytle et al., WO 00/35280 or Shytle et al., WO 00/35279, in view of Summers et al., Gastroenterology (Abstract).

Shytle teaches the administration of mecamylamine (N-2,2,3-tetramethylbicyclo-[2.1.1]heptan-2-amine), or an optical isomer thereof, in the treatment of gastrointestinal motility disorders, such as Crohn's disease, or spasmogenic intestinal disorders, such as irritable bowel syndrome. See claims 54 and 62, pages 28 and 29. Transdermal administrations are disclosed in claims 55 and 63. Dosages are taught on page 12, as a range of about 0.001 mg/kg to about 6 mg/kg per day of exo-S-mecamylamine. Compositions may be formulated to provide rapid, sustained or delayed release of the active agent, as well as by controlled-release means. Combinations with multiple release layers are presently conventional formulations. Such characterizations encompass the "modified-release formulation" requirement of instant claims 1 and 30. Shytle teaches the optically active forms of mecamylamine, as well as the racemic mixture, on pages 2-4. Shytle teaches optical purity is important in that one isomer may be active while the other is inert. One isomer may produce an adverse effect while the other does not. In the case of mecamylamine, little or no difference in potency or efficacy is noted. Papke et al., Journal of Pharmacology and Experimental

Therapeutics, cited herein for evidentiary purposes only, corroborates this finding. See the second column, page 652. In view of the well documented adverse effects resulting from the administration of racemic mecamylamine, the skilled artisan is provided motivation to seek an enriched or pure (R) or (S) enantiomer with which less, or no, adverse effects may occur.

Summers teaches significant inhibition of gastrointestinal propulsion in a mammalian model following mecamylamine administration. Such inhibition would have reasonably been a desired property in treating a functional bowel disorder, such as diarrhea-dominant irritable bowel syndrome, wherein patients suffer from an abnormal increase in gastrointestinal motility, or in treating an inflammatory bowel disease, such as Crohn's disease.

The claims differ with respect to optimal dosing ranges and dosing regimens. However, it is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(II). The determination of the optimum dosage regimen to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art, and such determination would have been made in accordance with a variety of factors. These would have included such factors as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology

profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered a part of a drug combination. Thus, in the absence of evidence to the contrary, the currently claimed specific dosage amounts and dosage regimens are not seen to be inconsistent those that would have been determined by the skilled artisan.

Multiple drug therapy is conventional practice in the treatment of gastrointestinal disorders characterized by an abnormal increase in motility. Testing in a U.S. Pharmacopeia (USP) Type 2 Apparatus under defined physical and chemical conditions is conventional practice to determine the pharmacokinetics of an active agent in a pharmaceutical formulation.

Neither Shytle nor Summers teaches peak:trough plasma level ratios, plasma concentrations as a function of time or release rates as a function of time.

However, determining such optimal pharmacokinetic and pharmacodynamic parameters is well within the purview of those skilled in the art of formulation chemistry through no more than routine experimentation. Applicant has merely discovered unknown properties for an old compound. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of unknown properties, i.e., pharmacokinetic properties, which are inherently present in the prior art does not make the present claims patentable. See MPEP § 2112.01. There is no requirement that a person of ordinary skill in the art would

have recognized the inherent disclosure at the time of the invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 67 USPQ2d 1664, 1668 (Fed Cir. 2003).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 30, 2008 /Phyllis G. Spivack/

Primary Examiner, Art Unit 1614